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By: Margaret M. Doss Printed: Margaret M. Doss

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Walker et al.
Title: **GENES ASSOCIATED WITH NEUROTRANSMITTER PROCESSING**

Serial No.:	09/786,136	Filing Date:	June 07, 2001
Examiner:	Moore, W.	Group Art Unit:	1652

Commissioner for Patents
Washington, DC 20231

DECLARATION UNDER 37 CFR 1.132 OF MICHAEL G. WALKER

I, Michael G. Walker, declare:

1. I received my doctoral degree from Stanford University, Stanford, CA in 1992. I have held the position of Consulting Professor in the Department of Medicine at Stanford University since 1995 and have consulted to Incyte Genomics since 1996. My work has involved the development of analytical tools for the characterization and annotation of molecules by their expression in relation to cellular function, disease, and metabolic pathways. I am the first named inventor on the pending application.

2. The application relates to polynucleotides that are surrogate markers for neurological disorders, in particular, for Parkinson's disease, schizophrenia, and neuroendocrine cancers which were identified by their co-expression with known diagnostic and prognostic markers.

3. I understand that the OFFICE ACTION presents 35 USC §§ 101 and 112 rejections of claims 1-8 and 11, directed to the described invention as not supported by a specific utility because "The specification states no specific *in vitro* utility for the polypeptide of SEQ ID NO:6, and indicates no specific *in vitro* utility for a nucleic acid encoding the polypeptide of SEQ ID NO:6".

4. The purpose of my declaration is to support the asserted utility of the identified polynucleotides and polypeptides as diagnostics. To that end, I will discuss the attached journal article of Thompson et al. (2002; Identification and Confirmation of a Module of Coexpressed Genes, Genomics Research 12:1517-1522) and the data presented in the application.

5. The relevant points of the Thompson et al. article are as follows:

a) Thompson et al. used guilt-by-association method (GBA, the method used in this application) across all tissues of the dbEST and UniGene databases to identify functional modules of gene expression data (all genes similarly expressed across all tissues).

b) The data set was tested and found to be reliable using ubiquitously expressed genes and known coexpressed genes.

c) A novel functional module was found to be involved in breast cancers.

d) Quantitative expression profiles of six of the genes identified in the novel functional module were confirmed using reverse transcriptase real-time PCR with four different cell lines derived from mammary epithelial tissue.

e) Published information on these six genes revealed interactions in two distinct classes: transcriptional control and ubiquitin proteasome pathway. Thompson et al. suggest that three of the genes in the first class regulate transcription of the three genes in the second class.

f) Thompson et al. stated that their work focused on a small subset of the available data and is expected to lead to the identification of many more functional modules.

g) Thompson et al. therefore provides independent evidence that the method of analysis used in the instant application to predict coexpression of genes is confirmed by actual measurements of the coexpressed genes in target tissues, and further provides evidence of functional relations between the coexpressed genes.

7. I will now point out the parts of the specification that support the asserted utility, that the claimed invention is diagnostic of neurological disorders.

a) The known genes used in the GBA analysis of the instant specification were characterized as to function and disease indication in EXAMPLE IV, pp. 19-21. In particular, secretogranin II is characterized at p. 20, lines 11-16, and cited references as a precursor for secretoneurin which is a "pronounced" stimulator of dopamine release and therefore a likely marker in dopamine related neurological disorders, such as Parkinson's Disease (Agneter, et al., reference # 1 of the IDS), as well as a useful marker for neuroendocrine based tumors (Fischer-Colbrie, et al., reference # 11, and Goodall et al., reference # 12 of the IDS). TH is described in the specification and the art of record as a controlling factor in the synthesis of the catecholamines dopamine and norepinephrine and closely related to the pathogenesis of neurological diseases such as dystonia and Parkinson's disease, and psychiatric diseases, such as schizophrenia (Nagatsu, reference # 29 of the IDS).

b) As recited in EXAMPLE V, Table 8 at p. 24, SEQ ID NO:4 (Incyte gene 282339) was found in

only 12 of 522 cDNA libraries examined, and was highly significantly coexpressed with four known neurotransmitter processing genes in these libraries, in particular, with secretogranin I and II, TH and hVMAT1.

c) The data therefore supports the asserted use of the claimed polynucleotides, in particular SEQ ID NO:4 and its encoded protein, SEQ ID NO:6, in the diagnosis or in monitoring the progress of therapeutic intervention for diseases associated with neurotransmitter processing, in particular, with Parkinson's disease, schizophrenia, and neuroendocrine cancers. See, in particular, the specification at p. 12, lines 2-11; and at p. 13, lines 11-22.

I hereby declare that all statements made herein are true and that they are based on my own knowledge, information and belief. These statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issued from it.

Date: 11/25/02

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